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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/390,740	02/17/95	COLEMAN R	

HM12/0907

LEGAL DEPARTMENT
INCYTE PHARMACEUTICALS, INC.
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EXAMINER	
MARSCHEL, A	
ART UNIT	**PAPER NUMBER**
1631	20

DATE MAILED: 09/07/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applic...(s)
08/390,740	Coleman et al.
Examiner	**Group Art Unit**
Ardin Marschel	1631

☒ Responsive to communication(s) filed on *Jun 5, 2000 (IDS)*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 5, 6, 13, 17, 18, 21-26, and 34-39* is/are pending in the applicat

Of the above, claim(s) *21-24, 34, and 35* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 5, 6, 13, 17, 18, 25, 26, and 36-39* is/are rejected.

☒ Claim(s) *2-4, 7-12, 14-16, 19, 20, and 27-33 have been canceled.* ~~are objected to~~.

☒ Claims *1, 5, 6, 13, 17, 18, 21-26, and 34-39* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, ~~Paper No(s).~~ *(1 sheet)*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

This application was previously suspended for a potential interference. Such interference proceedings are usually appropriate only if the claims are otherwise allowable. Due to the newly set forth rejections summarized hereinbelow, the indication of allowable claims is hereby withdrawn, the suspension is withdrawn, and prosecution is reopened. Applicants are also hereby informed that the amendment, filed 3/17/97, has been authorized for entry and has been entered.

It is noted that an Examiner Interview Summary for a conversation that occurred on 4/10/97 authorized an Examiner's amendment. Such amendments are only appropriate at the time of allowance. Due to the reopening of prosecution herein summarized and the withdrawl of the indication of allowability, that Examiner's Amendment, authorized 4/10/97, has not been entered.

Applicants' arguments, filed 3/17/97, have been fully considered and they are deemed to be persuasive to overcome rejections previously of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because no submission of the nucleotide sequence given in Figure 1 has been received on computer readable form or in the sequence listing in the specification. This Figure 1 nucleotide sequence is 291 nucleotides in length. It is noted that the sequence listing does contain a 289 nucleotide sequence as SEQ ID NO: 1, but is as noted only 289 nucleotides in length. Applicants are also hereby reminded that sequences in Drawings/Figures must be present in computer readable form etc., if they meet the sequence rule requirements, but that Drawings/Figures are not required to contain the sequence number therein such as "SEQ ID NO:__". Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Definitions: [from REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS; repeated from

http://www.uspto.gov/web/menu/utility.pdf]

"Credible Utility" - Where an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility. A *credible* utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for such use. For example, no perpetual motion machines would be considered to be currently available. However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers. Therefore, the credibility of such an assertion would not be questioned, although such a use might fail the *specific* and *substantial* tests (see below).

"Specific Utility" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context

of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

Note that "throw away" utilities do not meet the tests for a *specific* or *substantial* utility. For example, using transgenic mice as snake food is a utility that is neither specific (all mice could function as snake food) nor substantial (using a mouse costing tens of thousands of dollars to produce as snake food is not a "real world" context of use). Similarly, use of any protein as an animal food supplement or a shampoo ingredient are "throw away" utilities that would not pass muster as specific or substantial utilities under 35 U.S.C. § 101. This analysis should, or course, be tempered by consideration of the context and nature of the invention. For example, it a transgenic mouse was generated with the specific provision of an enhanced nutrient profile, and disclosed for use as an animal food, then the test for specific and substantial *asserted* utility would be considered to be met.

"Well established utility" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. "Well established utility" does not encompass any "throw away" utility that one can dream up for an invention or a nonspecific utility that would apply to virtually every member of a general class of materials, such as proteins or DNA. If this is the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as

> landfill, an amusement device, a toy, or a paper weight; any carbon containing molecule would have a "well established utility" as a fuel since it can be burned; any protein would have well established utility as a protein supplement for animal food. This is not the intention of the statute.

See also the MPEP at §§ 2107 - 2107.02.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 6, 13, 17, 18, 25, 26, and 36-39 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by either specific and/or substantial utility or a well established utility.

The claimed nucleic acids are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to a wide variety of nucleic acids. The specification states, in the section entitled "Detailed Description of the Invention" starting on page 8, that the nucleic acid compounds may be useful for diagnostic assay, hybridization probes, antisense nucleic acids, PCR amplification, gene mapping, isolation of homologous sequences, detection of gene expression, expression of protein, antibody production, specific inhibitors, agonists, antagonists, and other

effective means for treating problems of the pancreas. These are alleged specific uses which are applicable to a widely varying group of nucleic acids in general. It is also noted that chemokines are particularly discussed in the specification at several citations regarding their broad activities. For example, on page 3, line 9, through page 4, line 28, various chemokines are described with varying activities discussed. Particular attention is drawn to page 3, lines 14-15, wherein it is stated that chemokine activities demonstrate a high degree of target cell specificity. This statement is significant in that the subject matter of the instant claims is "not" characterized as to target cell specificity other than the generic pancreas location thereof. Numerous activities are carried out by the pancreas, including numerous non-chemokine activities, and thus this pancreas specificity is generic in nature, especially since the chemokines encoded by the instantly claimed nucleic acids have no asserted correlation to any particular disease or illness, but rather only speculated as being involved in a long list of diseases or illnesses. Thus, "real world" disease or illness condition correlation is absent for the claimed subject matter. No other alleged utility has been found as filed.

Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein

could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted

utility would be well established for the compounds. In the instant specification in the paragraph bridging pages 4 and 5 there is set forth a research proposal for "new diagnostic techniques" and for "use in the development of effective therapies". As noted above in the basic summary of insufficient bases for utility, items A - E reasonably summarize the lack of patentable utility of the instant invention as filed. It is noted that a number of examples have been set forth for the basic isolation and characterization of PANEC-1 and PANEC-2 starting in the instant specification on pages 14-17. From pages 17-28 of the specification a review of generic methods are given with only speculation as to what specific or substantial effects are connected to PANEC-1 or PANEC-2. These are also clearly research proposals which lack patentable utility. In summary, the instant invention, as filed, has not been set forth with a patentable utility due to a lack of specific, substantial, or well established utility.

Claims 1, 5, 6, 13, 17, 18, 25, 26, and 36-39 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claims 38 and 39 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for

hybridization probes of SEQ ID NOs: 1 or 3, does not reasonably provide enablement for any nucleotide sequence from claims 36 or 37. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The stringent hybridization limitation in claims 36 and 37 results in numerous oligonucleotides as well as longer nucleic acids which are within the scope of these claims due to exact

sequence matching or alternatively matching with the content of a few percent mismatching nucleotides to the nucleic acids of SEQ ID NOs: 1 or 3. Numerous of these oligonucleotides will also present exact sequence matches to non-PANEC nucleic acids, especially oligomers of short length. See, for example, prior art rejections set forth below regarding such matching oligonucleotides. In order to reasonably perform the methods of instant claims 38 and 39 the hybridization probes used therein must be selected so as to result in the correlation as stated in these claims. The instant application has failed to set forth any selection criteria. It is noted that hybridization design is generically known in the art, however, such design is reasonably performed only after a selection criteria is set forth by which to screen out undesireable, yet sequence matching, potential hybridization probes. Negative control nucleic acids may be used for such a selection criteria. No negative control nucleic acids have been proposed or are clearly apparent from the instant application. Instant Figure 3 shows some chemokine relatives which have sequence similarity at the amino acid level but nowhere is there an analysis as to what sequence similarity is present at the nucleic acid level for these relatives compared to PANEC sequences. It is well known that the third base in each codon may, and generally does, vary from protein to protein coding sequence. Thus, even matching amino acid segments from said Figure 3 may unpredictably be anywhere from 67% to 100%

similar to PANEC sequences and thus are unpredictable for negative control usage. In summary, the only sequences that have been instantly set forth which would be predictably used as hybridization probes are the full sequences of SEQ ID NO: 1 or 3, with others beyond these being unpredictable regarding correlative capability as required in instant claims 38 and 39.

Claims 1, 5, 6, 13, 17, 18, 25, 26, and 36-39 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while providing written description enablement SEQ ID NOs: 1 and 3, does not reasonably provide written description enablement for genomic sequences etc. as summarized below. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The specification discloses SEQ ID NOs: 1 and 3 which correspond to the cDNA encoding the PANEC-1 and PANEC-2 protein species, respectively. It is noted that cDNA cloning resulted in illucidating said SEQ ID NOs: 1 and 3 as given in the instant specification on pages 15-16, but that section V on page 17 lacks disclosure of a full length gene sequence. SEQ ID NOs: 1 and 3 per se meet the written description and enablement provisions of 35 USC 112, first paragraph. However, the above listed claims are directed to encompass full gene sequences, sequences that hybridize to SEQ ID NOs: 1 or 3, corresponding sequences from other species, mutated sequences, allelic variants, splice

variants, and so forth. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOs: 1 and 3, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical

invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NOs: 1 and 3 but not the full breadth

of the claims meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36 and 37 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Esposito et al. (JBC, Vol. 263, pp. 11466-11472[1988]).

Instant claims 36 and 37 are limited to nucleic acid sequences which are capable of hybridizing to the nucleic acids of SEQ ID NOs: 1 and 3, respectively, under stringent conditions. Generally, stringent hybridization conditions require a high percentage of complementarity in the range of 90-100% for stable hybridization. Such complementarity is shown below for two sequences from the reference which are capable of hybridization to each of the instantly cited sequences under stringent hybridization conditions as follows:

reference seq 5(Table I, page 11468) 3'-GGGGGCCCCC-5'
||||| ||||
instant SEQ ID NO: 1: 5'...CCCCCAGGGG...3'
(bases 54-63)

complementarity at 9 of 10 bases = 90%

or

reference seq 1(Table I, page 11468) 3'-CCCCCGGGGG-5'
||||||| ||
instant SEQ ID NO: 3: 5'...GGGGGCCTCC...3'
(bases 321-330)

complementarity of 9 of 10 bases - 90%

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 29, 2000

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER